Pfizer Inc.	CP-945598 (otenabant)
Mechanism of Action	Cannabinoid receptor 1 (CB1) antagonist http://iuphar-db.org/DATABASE/ObjectDisplayForward?objectId=56 http://www.ncbi.nlm.nih.gov/gene/1268
Overview	CP-945598 is a high affinity (Ki = 0.75 nM), selective (~10,000 x over CB-2), competitive antagonist of the human and rat CB-1 receptor. It inhibits both basal and cannabinoid agonist-mediated CB-1 receptor signaling. CP-945598 reduces acute food intake in rodents, decreases food intake and body weight in obese Beagle dogs, and acutely stimulates energy expenditure in rats.
Safety/Tolerability	The overall clinical experience with CP-945598 has been positive through Phase 2 into Phase 3. The primary side effects are nausea, vomiting, diarrhea, loose stools, dizziness, headache, hiccups, abdominal pain, fatigue, insomnia, somnolence, pruritus and decreased appetite. Suicidal thoughts and behavior (suicidality) have been reported for another CB-1 antagonist (rimonabant). Psychiatric adverse events, including depression, depressed mood, anxiety and suicidal ideation have been reported with CP-945598. Most of the observed side effects were mild to moderate in severity and resolved quickly. CP-945598 is neither embryolethal nor teratogenic in rats and rabbits at maternally toxic doses.
Additional Information	CP-945598 significantly reduced food intake and body weight in overweight to obese subjects with hypertension or dyslipidemia over 6 weeks to 6 months administration.
Suitable for and Exclusions	Benefit/risk is most plausible in acute, sub-acute and/or high morbidity indications given the potential for psychiatric adverse effects.
Clinical Trials	http://www.clinicaltrials.gov/search?term=%22CP-945,598%22
Publications	http://www.ncbi.nlm.nih.gov/pubmed?term=CP-945%2C598 http://dmd.aspetjournals.org/content/39/12/2191.full.pdf+html http://pubs.acs.org/doi/pdfplus/10.1021/jm8012932